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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/041,491	03/12/98	SCHWABE C	07842.047.99

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EXAMINER	
GUPTA, A	

ART UNIT	PAPER NUMBER
1654	8

DATE MAILED: 03/04/99

Please find below and/or attached an Office communication concerning this application or proceeding.

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This is a communication from the examiner in charge of your application. DATE MAILED:
COMMISSIONER OF PATENTS AND TRADEMARKS

■ This application has been examined ■ Responsive to communication filed on 12-7-98 ■ This action is made final.

A shortened statutory period for response to this action is set to expire 3 Months from the date of this letter.
Failure to respond within the time period will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENTS ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ■ Claims 4-6, 11-12, 14-20 are pending in the application.
   Of the above claims, 11-12 are withdrawn from consideration.
2. ☐ Claims ___ have been cancelled.
3. ■ Claims 20 are allowed.
4. ■ Claims 4-6, 14-19 are rejected.
5. ☐ Claims ___ are objected to.
6. ☐ Claims ____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on ____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on ____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on ____ has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under 35 USC 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. ____; filed on ____.
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

09/041,491

DETAILED ACTION

1. Applicant's election without traverse of Group I, claims 4-6, in Paper No. 7 is acknowledged.

Claims 11-12 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected Group II.

A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112
First Paragraph

3 Claims 4-6 remain and newly added claim 14-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons set forth in the previous office action and the reasons set forth below.

Applicants argue that specification is fully enabled since the specification teach number of different assay for routinely testing the relaxin activity of these peptides. Moreover, the reliance on Yuen et al. to support allegation that the properties of peptides in an in vitro system do not necessarily correlate to in vivo success is misplaced. Applicants submit "that merely because some therapies after extensive clinical trials, are found to have side effect that are intolerable with commercialization of the therapy cannot be automatically extended to all therapies." In vitro studies provide basic biochemical information about cellular response. Applicants further state that rejection relied upon is not an enablement rejection, rather the rejection is a utility rejection under § 112. Under the utility guidelines, all that is required is a reasonable correlation between the effectiveness of the methods and the asserted use. In the present case, applicants state, the specification has provided experimental data which demonstrates that the peptides used according to the claimed methods are effective in: maintaining sperm motility; inhibiting collagen production in vitro; inhibiting fibronectin production in vitro; activating expression of procollagenase; and pubic ligament softening in mice. "Applicants submit that the disclosure of the specification provides a reasonable correlation between the effectiveness of

the peptides utilized according to the claimed methods and the use of these methods to treat a medical condition that is ameliorated by treatment with relaxin."

Applicant submit, for the breathe of the claims, that amended claim 4, which now recites that the condition is ameliorated or prevented by the administration of relaxin like factor. Amelioration in this context is any type of Amelioration of a symptoms that is art recognized as treatment and patent law does not require and applicant to detail the precise mechanism of the invention.

For the working examples, applicants state that the guidelines for enablement do not demand and the Applicants to obtain positive Phase II clinical result. The in vitro and animal models of activity presented by Applicants suffice to establish the utility of the claimed methods.

Applicant's arguments filed 12-7-98 have been fully considered but they are not persuasive.

First, the rejection is made is not a rejection under utility rather the rejection is made under 112 enablement. It is acknowledge, as applicants have pointed, the specification is fully enabled for maintaining sperm motility; inhibiting collagen production in vitro; inhibiting fibronectin production in vitro; activating expression of procollagenase; and pubic ligament softening in mice. It is however the scope of the claims that is not fully enable. The disorder that are cited by the applicants include neurodegenerative and neurological disease, depression, hair loss, cardiovascular diseases. The newly amended claims now not only to the treat such conditions, but they prevent such conditions (this issue will be addressed below). As applicants have pointed out, the specification has provided guidance for maintaining sperm motility; inhibiting collagen production in vitro; inhibiting fibronectin production in vitro; activating expression of procollagenase; and pubic ligament softening in mice. However, it is unclear how these activities are correlated with treating various cardiovascular disorders and neurological disorders. Nothing in the specification would demonstrate, in-vitro or in-vivo, data that relaxin like factor would be effective in ameliorating the conditions of a neurological disorders, such as ALS. Applicants have not submitted any art that would indicate that maintaining sperm motility; inhibiting collagen production in vitro; inhibiting fibronectin production in vitro; activating expression of procollagenase; and pubic ligament softening in mice are well established and well correlated tests for concluding the effectiveness to treat cardiovascular and neurological disorders. It should be noted that Yeun was cited to demonstrate the difficulty associated extrapolation of in-vitro testing to in-vivo effectiveness for Neurological disorders. In the

instant application, the specification is void of any data, including in-vitro testing, to clearly demonstrate that relaxin like factors are effective in treating neurological disorders and cardiovascular disorders. The extent to which these disorders are discussed in the specification are on pages 6, lines 2-9, where the treatment of the disease is associated with the activation of biological function associated with binding with relaxin or RLF receptor and on page 13, lines 20-26 where a conclusion from the activity of relaxin, a structurally distinct peptide, is extrapolated to relaxin like factor. Beyond this, the specification does not address the treatment of these disorders in any manner. There is no description to which cardiovascular disorders and/or neurological disorders relaxin like factor can be associated with. Furthermore, it is improper to conclude that the activity associated with a structurally distinct compound would also be associated with this compound., as reflected by the Rudinger article. It should be noted that RLF belongs to a family of insulin like hormones which include insulin, relaxin and IGF. Even though the insulin and relaxin belong to the same family, the activity associated with insulin is quite different from the activity associated with relaxin. For example, the art does not recognize the ability of insulin to treat alopecia and similarly the art does not recognize the ability of relaxin to treat diabetes. Thus clearly a extrapolation can not be made for activity of one compound from a second compound where the second compound is structurally distinct. The newly amended claims also state the prevention of the claimed disorders. However, the specification has not enabled prevention of any of the disorders claimed including infertility. Do applicants intend to mean that the relaxin like factor is effective in preventing neurological disorders such as ALS and Alzhiemer's. Currently, no therapy exists which would be effective in preventing these disorders. What kind of cardiovascular diseases can be prevented from RLF? For hair loss, it is known hair growing agents are known to have an effect where villus hairs still exist. However, the art has not recognized the growth of hair follicles for those patients that have suffered form mail patter baldness for long period of time and thus are unable to grow vellum hair follicles. Does RLF prevent the loss of villus hair? Applicants have not addressed any issues for the disorders claimed that would demonstrate prevention can be achieved. This includes infertility of claim 16. For support of this claim, applicants make reference to page 37, lines 22-32. On this page an assay to demonstrate the ability of RLF to preserve motility of human sperm is disclosed. Nothing in the on this page demonstrates that the RLF can prevent infertility for both men and women. In fact, the specification is void of any guidance on how prevention of infertility is achieved. Thus, the specification is clearly not enabled for preventing any of the disorders cited by applicants.

Applicants are suggested to omit preventing from the claims to simplify the issues.

2. Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim is drawn to a method of ameliorating or preventing immature ripening of the cervix.

However, it is unclear what is the intended meaning of immature ripening of the cervix. What is the intended meaning of immature and ripening. No definition for this terminology exists in the pages cited by the applicants for support of this claim.

3. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anish Gupta whose telephone number is (703) 308-4001.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can normally be reached on (703) 308-0254. The fax phone number of this group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Cecilia J. Tsang
Supervisory Patent Examiner
Technology Center 1600